

EFFECT OF "LIDOCAINE" INFUSION ON SEVOFLURANE REQUIREMENT DURING BIS GUIDED CARDIAC SURGERY

NAGHAM HASHIM¹ & ABDULRAHMAN SAEED²

¹Anesthesia and intensive care Department / Surgeries Hospital Specialist - Heart
Center (EMC) / Baghdad medical College / University of Baghdad, Iraq

²Anesthesia and intensive care Department/ Al Alam General Hospital/ Baghdad medical
College / University of Baghdad

ABSTRACT

The background

The need for sevoflurane is reduced in the patients by intravenous lidocaine, in an amazing way when compared to the patients who did not obtained lidocaine. The double-spectrum indicator is a non-interventional device. When anesthesia is given for the patients during surgery or severe diseases or injuries, the brain-mapping device is used to indicate the patients' severity. This is done by reversing the signals, received by the device.

The reason of the study

The effect of lidocaine, when added to the amount of sevoflurane administered to the patients is demonstrated in this study. The tests are done by comparing the lidocaine received patients, with the patients who were given sevoflurane without lidocaine, with the use of the double-spectrum indicator.

Pathology and Methods of Work

The research was performed from June 2014 to December 2014 at the Erbil Center for Cardiothoracic Surgery with 50 patients, who were separated into two different groups. Lidocaine was administered to the first group of 25 patients and the second group of 25 patients was not treated with lidocaine.

Results

In group A patients, the rate of sevoflurane concentrations was 1.68. This reduced to 1.44% at sternotomy and 1.2% during bypass. The rate of sevoflurane administered in group B was 1.36%, as soon as anesthesia was given. This has reduced to 0.84% at sternotomy and 0.4 during bypass.

Conclusions

The amount of sevoflurane that needs to be administered to the patients through assessment using the double-spectrum indicator is drastically reduced by the intravenous use of lidocaine, while giving anesthesia.

KEYWORDS: Sevoflurane, Lidocaine Received & Anesthesia

Received: Oct 17, 2017; **Accepted:** Nov 07, 2017; **Published:** Dec 27, 2017; **Paper Id.:** IJMPSFEB20182

INTRODUCTION

Bispectral Index

Previously, the effects of anesthetics on the brain were not monitored by the anesthesiologists, in terms of

"adequacy" or "depth" of anesthesia. Indirect assessment has been done on sedation by using subjective sedation or vital signs scales. However, under-sedation and over-sedation remains a major challenge, due to the restrictions in the subjective assessment tools. It is assumed that the consciousness is blocked by general anesthetics by suppressing the central nervous system. It is anticipated that the anesthesia's adequacy is related to some components of the electroencephalogram (EEG), since it measures the electrical motion of the brain. The hypnotic element of a continuous EEG parameter is the bi spectral index (BIS) that ranges from an awake, no drug effect value of 95 to 100 to no measurable activity of EEG with a zero value.

The BIS monitor system includes a digital signal converter, a sensor, and a monitor. The electrical signals are picked up from the cerebral cortex by the sensor and passed on to the digital signal converter. Then, the digitized signals move to the pre-processor of the device, which screens the "artifacts" (stray high-frequency signals), which are formed as a result of electro cautery equipment or patient movement. To determine the bi spectral index, the filtered EEG data is then subjected to a sophisticated algorithm, which is in the numerical level between 0-100. The BIS readings are as follows: 90-100 = fully awake; 80-90 = light sedation; 60-80 = moderate sedation; 40-60 = deep sedation; 0 = no EEG activity;

It has been recommended that the BIS can be used for titrating volatile anesthetics accurately according to specific requirements. This helps to ensure that the exposure to unwanted increased concentrations of anesthetics while decreasing the chances of mindfulness during anesthesia.

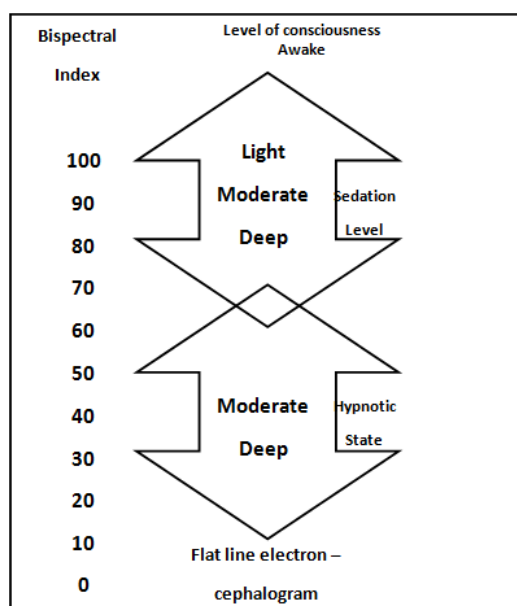


Figure 1: Diagrammatic Representation of BiSpectral Index Values

LIDOCALNE

Pharmaeokinetics

As a local anesthetic, the efficiency of lidocaine is categorized by a speedy action in-between the period of efficacy. Thus, lidocaine is appropriate for block, infiltration, and surface anesthesia. Numerous available formulations can be utilized before intubations, endoscopies, etc. pH buffering of lidocaine results in less painful local freezing. For short ophthalmic procedures, lidocaine drops are used on the eyes.

Lidocaine is one of the most significant class-Ib antiarrhythmic drug; for treating ventricular arrhythmias (for digoxin poisoning, cardio version, acute myocardial infarction, and cardiac catheterization) it is used intravenously if amiodarone is contraindicated or not available. For this indication, it should be given after defibrillation. Vasopressors and CPR have been started. Lidocaine can be used as a cough suppressor (antitussive). When inhaled, it acts peripherally and reduces the reflex of cough.

This application can be used as a security and relief for intubated patients, since it decreases the coughing frequency and any other damage to trachea, it could cause when developing from anesthesia.

Pharmacodynamics

Signal conduction in neurons is altered by anaesthesia lidocaine by hindering the speed voltage-gated Na⁺ channels in the cell membrane of neurons that are accountable for the propagation of signal. With adequate blockage, the postsynaptic neuron's membrane will not depolarize and therefore will fail to conduct an voltage-gated Na⁺ channels. The anesthetic effect is created by not only avoiding pain signals from spreading to the brain, but also by preventing them before they could start. A high degree of selectivity is allowed by the cautious titration in the sensory neurons' blockage, whereas advanced concentrations also affect neuron signaling's other modalities.

Antiarrhythmic

For the action of drug in the heart, the same principle is applied. The depolarization threshold is raised by blocking the sodium channels in the conduction system as well as the heart's muscle cells, which will make the heart to decrease to start or perform early action of 241 potentials that causes an arrhythmia.

Sevoflurane

Pharmacology

Sevoflurane acts mainly as GABA_A receptor's positive allosteric modulator. It also potentiates glycine receptor currents, acts as an antagonist for NMDA receptor, inhibits nACh and 5-HT₃ receptor. Sevoflurane is breath in as an aesthetic, which is used to make children asleep during surgery. However, while waking up from the medication, it is observed that it causes delirium and agitation. Still, it is not known whether this can be stopped.

Pharmacokinetics

Among the recently released anesthetics for clinical use, Sevoflurane is comparatively added recently to the range of inhaling aesthetics. When compared to the older inhalational agents such as halothane or isoflurane, the most significant property of sevoflurane is that it is less soluble in the blood. The effects are rapid uptake and stimulation than the other inhalational agents, faster removal and rescue, and improved depth control of an aesthesia. The faster pharmacokinetics is an outcome of the gas partition/ low blood coefficient of 0X9. The minimum alveolar concentration (MAC) of sevoflurane is 2.05%, with an oil/gas partition coefficient of 47.2. Liver metabolizes 2-5% of the drug utilized. The pharmacokinetics of sevoflurane do not change in obese patients, children and in patients with renal insufficiency.

Mask induction is made feasible by pharmacokinetics and pleasant odour of sevoflurane, which is a benefit in pediatrician aesthesia. The formation of inorganic fluoride is resulted from the hepatic metabolism of sevoflurane. A minor amount of sevoflurane is decreased upon contact with alkaline CO₂ absorbent, and the

formation of a metabolite (compound A) is seen, which is inhaled in minor amounts. The question whether the compound A and inorganic fluoride are nephrotoxic is currently a subject of controversy.

Pharmacodynamics

Sevoflurane is an inhalation anesthetic agent that is used for induction and for maintaining general anesthesia. The administration of Sevoflurane is connected with a smooth, fast loss of consciousness during inhalation and a rapid retrieval when anesthesia is discontinued.

For a 40-year-old adult, minimum alveolar concentration (MAC) of sevoflurane in oxygen is 2.1%. The MAC of sevoflurane reduces with the addition of nitrous oxide and with age.

Induction is accompanied with a minimum of upper respiratory irritation signs or excitement, no central nervous system stimulus and no indication of too much secretion within the trachea bronchial tree. Inspired concentration is rapidly followed by the changes in the depth of sevoflurane anesthesia. Induction and recovery times were decreased in child patients who received sevoflurane.

Adverse Effects

Intracranial pressure is raised by sevoflurane and it can lead to respiratory despair. Studies inspecting a current important health concern, neurotoxicity induced by anesthetics (includes sevoflurane, especially with infants and children) are troubled with confounders, and most are statistically underpowered, and so are debated to request more data either to back up or contradict the potential link.

The safety of anesthesia when used in infants and children is concerning. The preclinical evidence from appropriate animal models have shown that the commonly used clinical essential agents, including sevoflurane, could turn to be neurotoxic to the developing brains, thus, causing neurobehavioral anomalies in the elongated term. As of 2010, two studies, PANDA and GAS (large-scale clinical studies) are going on; to supply further important data on neuro developmental effects of general anaesthesia on young children and infants, even when sevoflurane is used.

PATIENTS AND METHODS

Study Population

This study was conducted from June 2014 to December 2014 in Erbil cardiac center after getting permission from its ethical committee. For this study, 50 patients were selected as the candidates. Selection was done with exclusion criteria consisting of patients with history of seizures, patients with history of lidocaine reaction, or the ones using drugs that affect BIS. Standard monitors were used including non-invasive and invasive arterial pressure, ECG, central venous pressure and pulse oximetry. BIS was also used to evaluate anesthesia's depth. Anesthesia was induced after 8 hours of fasting using fentanyl 2 mcg/kg i.v. followed after 3 min by propofol 1.5 -- 2.5_1 mg kg_1 iv. When BIS touched less than 50, atracurium 0.5 mg kg i.v. was given to permit tracheal incubation. With a tidal volume of 7-8 ml/kg and an oxygen fraction of 0.4 in air, the lungs were ventilated. To maintain an end tidal CO₂ between 30 and 35 mm Hg, the respiratory rate was adjusted.

Patients were randomly distributed into 2 groups. Group B patients received 1.5 mg/ kg bolus of 2% lidocaine i.v. followed by 2 mg/kg/h infusion, whereas the patients in group A received saline in equal volumes.

The concentration of Sevoflurane was adjusted to keep BIS between 40 and 60 during anesthesia maintenance. Sevoflurane was decreased or increased by 0.5% if BIS goes out of the range. End-tidal sevoflurane concentration and BIS values were also noted as per the stages of the surgery. Lidocaine and sevoflurane were discontinued, before the Cardiopulmonary Bypass. Using independent t-test, normally distributed continuous data were analyzed.

A P value of < 0.05 was measured as statistically significant.

Demographics and Statistical Analysis

To collect the data, a data collection sheet was designed (Fig. 6). The collected information was managed via SPSS v.19 computer program. From each parameter, data was expressed as mean \pm standard deviation. The measure for statistical significance is independent t- test at p value < 0.05.

Table 1: Data Collection Sheet

Name: age: sex: weight: Group:

Date of operation: Type of operation:

	T1	T2	T3	T4
BIS				
Et sevoflurane				

RESULTS

Among the 50 patients involved in our study, 9 (18%) were female and 41 (82%) were male. Mean weight was 74.2 and the mean age was 65.26 \pm 34.22 years.

50 patients were separated into 2 groups: Control (A) group (n= 25) and Lidocaine (B) group (n=25). In this study, no patients were excluded. As per the data available in table 2, the mean dose of total bolus and infusion lidocaine was 398 \pm 11(mg). Immediately after induction of anesthesia, the mean concentration of Sevoflurane in the control group (A) was 1.68, 1.2 at pre-cardiopulmonary bypass stages and 1.44 at sternotomy.

In the lidocaine group (B), the mean concentration of Sevoflurane was 1.36 directly after anesthesia induction, 0.4 at pro-cardiopulmonary Bypass stages and 0.84 at sternotomy (see table 3).

A significant difference was observed between the 2 groups based on the independent t-test concerning the doses of sevoflurane immediately after induction of anesthesia, sternotomy and pro-cardiopulmonary Bypass stages.

Table 2: Patients and Lidocaine Parameters

Parameter		Control (group A) (N=25)	LIDOCIANE (GROUPE B) (N=25)	Total (n=50)
Age (Years)		67.32 \pm 28.3	65.92 \pm 30.2	65.26 \pm 34.2
Weight (Kg)		78 \pm 3	73 \pm 3	76 \pm 2
Gender	Male	21(84%)	20 (80%)	41 (82%)
	Female	4(16 %)	5 (20%)	9(18%)
Lidocaine dose			398 \pm 11	

Table 3: Mean Dose of Sevoflurane

Stage of Operation	Control (Group A) (n=25)	Lidocaine (group B) (n=25)
Immediately after induction of anesthesia	1.68+0.25	1.36+0.1
Sicrnotomy.	1.44+0.06	0.84+0.07
Pre-cardiopulmonary Bypass	1.2+0.1	0.4+0.01

DISCUSSIONS

This research shows that when lidocaine is given at a dose of 1.5 mg/ kg bolus followed by 2 mg/ kg/ h, it reduces the requirement of sevoflurane while keeping the BIS score between 40 and 60, during anesthesia maintenance in patients going through cardiac surgeries.

In this research, a significant statistical difference between the 2 groups have been found, which approve Wilson ET at who noticed in a research that lidocaine, without or with ketamine considerably decreased the MAC of sevoflurane in dogs.

Matsubara et al. also observed that intravenous lidocaine reduced MAC of sevoflurane in the dogs that are anesthetized. Another study showed that, lidocaine dose reduced the MAC of Sevoflurane in cats (Pypendop and Ilkiw).

The research conducted by us doesn't agree with Ahmed M. Omar et al. as it shows no statistical difference of MAC of sevoflurane between the 2 groups in human.

When cardiac surgery is performed for the patients included in this research, there was a reduction in ET sevoflurane during the operation or along the stages of operation, also due to the use of fentanyl 10 meg/kg/dose with midazolam 10 mg dose at sternotomy. Due to lidocaine's action at the spinal level, by reducing the motor response, the effect of lidocaine on MAC of Sevoflurane is noted.

However, it was detected that the intravenous infusion of lidocaine decreased the requirement of bispectral index-guided sevoflurane during anesthesia.

The rate of infusion of lidocaine and the bolus dose used in this research was (398 + 11 mg) that was on par with the earlier studies which showed that this dosage did not end in plasma concentration more than 4 Meg/ ml, which is less than the toxic levels.

CONCLUSIONS

During the maintenance of general anesthesia, intravenous administration of lidocaine can significantly reduce the requirements of BIS-guided sevoflurane

REFERENCES

1. Fitz-Henry, J (Apr 2011). "The ASA classification and peri-operative risk", *Ann R.CollSurgEngl* 93 (3): 185-187.
2. Long CW (1849). "An account of the first use of Sulphuric Ether by Inhalation as an Anesthetic in Surgical

Operations; Southern Medical and Surgical Journal 5: 705-13. Retrieved 2010-09- 13.

3. Anesthesia. Merriam-Webster. Retrieved 2012-06- 13
4. Matsuki A (2000). *"New studies on the history of anesthesiology-- a new study on Seishu Hanaoka's
"NyuganCkikenR.oku" (a surgical experience with breast cancer)". Masui: the Japanese Journal of
Anesthesiology 49 (9): 1038-43*
4. Ananthakrishnan, A Descriptive Study to Assess the Knowledge Regarding the Effect of Yoga in Reducing the Risk of
Cardiac Diseases among Adults in Selected Urban Areas of Tumkur with a View to Develop an Information
Guidesheet, International Journal of Medicine and Pharmaceutical Sciences (IJMPS), Volume 6, Issue 6, November -
December 2016, pp. 19-30
5. Niemegeers CIE, Janssen PAJ (1981). *"Alfentanil (R39209)-a particularly short- acting intravenous narcotic
analgesic in rats''. Drug Development Research 1: 830-8*
6. Cooper, RM; Pacey, JA; Bishop, MJ; McCluskey, SA (2005). *"Early clinical experience with a new
videolaryngoscope (GlideScope) in 728 patients". Canadian Journal of Anesthesia 52 (2): 191-8.*
7. Henderson, JJ (2003). *"Development of the 'gum-elastic bougie"'. Anaesthesia 58 (1): 103.-4.*
8. arter, Anthony J. (18 December 1999). *"Dwale: an anaesthetic from old England". BMJ 319 (7225): 1623--
1626.*
9. Ekman A, ct al. Reduction in the incidence of awareness using BIS monitoring, *ActaAnaesthesiologyScand*, January
2004; 48(1): 20-26.
10. Li XJ, Kang Y and Zhang C. [A study of bispectral index monitoring in assessing the depth of sedation of patients under
mechanical ventilation]. *Zhongguo Wei Zhong Bing Ji Jiu YiXue* 2009; 21(6): 361-363.
11. Johansen JW, et al. Development and clinical application of electroencephalographicbispectrum monitoring,
Anesthesiology, November 2000, Vol. 93, No. 5.
12. O'Connor MF, et al. BIS monitoring to prevent awareness during general anesthesia,*Anesthesiology*, March
2001; 94(3): 520-522
13. Sebel PS, et al. The incidence of awareness during anesthesia: A multicenter United States study, *Anesthesia Analg*
2004; Vol., 99, p. 833-839
14. Cepeda MS, Tzortzopoulou A, Thackrey M, Hudcova .I, Arora Gandhi P, Schumann R (2010). *"Adjusting the pH
of lidocaine for reducing pain on injection". Cochrane Database Syst Rev (12)*
15. Khaliq W, Alam S, Puri N (2007). *"Topical lidocaine for the treatment of postherpetic neuralgia". Cochrane Database Syst Rev (2)*
16. Kalciglu MT, Bayindir T, Erdem T, Ozturan O. (2005). *"Objective evaluation of the effects of intravenous
lidocaine on tinnitus.". Hearing Research 199 (1-2): 81-8.*
17. Birsa LM, Verity PG, Lee RP (May 2010). *"Evaluation of the effects of various chemicals on discharge of and
pain caused by jellyfish nematocysts". Comp. Biochem. Physiol. C Toxicol. Pharmacol. 151 (4): 426-30.*
18. Minogue SC, Ralph J, Lampa MI (Oct 2004). *"Laryngotrachealtopicalization with lidocaine before intubation
decreases the incidence of coughing on emergence from general anesthesia.".Anesthesia and Analgesia 99 (4):
1253-7.*

19. Morabito R, Marino A, Dossena S, La Spada G (Jun 2014). "Nematocyst discharge in Pelagianoctiluca (Cnidaria, Scyphozoa) oral arms can be affected by lidocaine, ethanol, ammonia and acetic acid.". *Toxicon : official journal of the International Society on Toxinology* 83: 52-8. doi:10.1016/j.toxicon.2014.03.002.
20. Reilly TJ (1999). "The Preparation of Lidocaine". *Journal of Chemical Education* 76 (11): 1557
21. Birsa LM, Verity PG, Lee RF (May 2010). "Evaluation of the effects of various chemicals on discharge of and pain caused by jellyfish nematocysts". *Comp. Biochem. Physiol. C Toxicol. Pharmacol.* 151 (4): 426-30. doi:10.1016/j.cbpc.2010.01.007. PMID 20116454.
22. Carterall, William A. (2001). "Sodium Channels and Neuronal Hyperexcitability". *Novartis Foundation Symposia* 241. p. 206.
23. Sheu SS, Lederer WJ (Oct 1985). "Lidocaine's negative inotropic and antiarrhythmic actions. Dependence on shortening of action potential duration and reduction of intracellular sodium activity.". *Circulation research* 57 (4): 578-90.
24. Lewin NA, Nelson LH, Antidysrhythmics". In Flomenbaum N, Goldfrank LR, Hoffman RL, Howland MD, Lewin NA, Nelson. LH. *Goldfrank's Toxicologic Emergencies*. New York: McGraw-Hill. pp. 963-4. 8 th ed.
25. "Lidocaine Hydrochloride and 5% Dextrose Injection". *Safety Labeling Changes*. FDA Center for Drug Evaluation and Research (CDER). January 2014.
26. "Lidocaine Viscous: Drug Safety Communication -Boxed Warning Required - Should Not Be Used to Treat Teething Pain". FDA Center for Drug Evaluation and Research (CDER). June 2014.
27. "Table 96-4 Drugs and Porphyria". *Merck Manual*. Merck & Company, Inc. 2011.
28. "Lidocaine - NO1BB02". *Drug porphyrinogenicity monograph*. The Norwegian Porphyria Centre and the Swedish Porphyria Centre. strong clinical evidence points to lidocaine as probably not porphyrinogenic
29. Khan, M. Gabriel (2007). *Cardiac Drug Therapy* (7th ed. ed.). Totowa, NJ: Humana Press.
30. Jackson II, Chen AR, Bennett CR (October 1994). "Identifying true lidocaine allergy". *J Am Dent Assoc* 125 (10): 1362-6.
31. *Australian Medicines Handbook*. Adelaide, S. Aust: Australian Medicines Handbook Pty Ltd. 2006.
32. Chowdhry S, Seidenstricker L, Cooney DS, Hazani R, Wilhelmi BJ (Dec 2010). "Do not use epinephrine in digital blocks: myth or truth? Part II A retrospective review of 1111 cases.". *Plastic and reconstructive surgery* 126 (6): 2031-4.
33. Basch R (2008). *Disposition of Toxic Drugs and Chemicals in Man* (8th ed.). Foster City, CA: Biomedical Publications. pp. 840-4.
34. Picard .I-; Ward SC, Zumpe R, Meek T, Barlow .I, Harrop Griffiths W (February 2009). "Guidelines and the Adoption of 'lipid rescue' therapy for local anesthetic toxicity". *Anaesthesia* 64 (2): 122-5.
35. "Lidocaine Ointment Prescribing Information". *Drugs.com*. Retrieved January 22, 2012.
36. "Solarcaine". Schering-Plough Healthcare Products, Inc. Retrieved July 27, 2009.
37. "Lidoderm (Lidocaine Patch 5%)". *Our Products*. Endo Pharmaceuticals. Retrieved 18 October 2012.

38. Bernardo NP, Siqueira MEPB, De Paiva MJN, Maia PP (2003). "Caffeine and other adulterants in seizures of street cocaine in Brazil". *International Journal of Drug Policy* 14 (4): 331-4.
39. <https://online.sepocrates.com/u/104316/lidocaine/Drug-I-Interactions>. Retrieved April 2014.
40. Jurgen Schaller; Helmut Schwilden (8 January 2008). *Modern Anesthetics*. Springer Science & Business Media. pp. 32
41. Brosnan, Robert J; Thiesen, Roberto (2012). "Increased NMDA receptor inhibition at an increased Sevoflurane MAC". *BMC Anesthesiology* 12
42. Patel SS, Goa KL. Sevoflurane: a review of its pharmacodynamics and pharmacokinetic properties and its clinical use in general anaesthesia. *Drugs* 1996; 51: 658-700
43. Quasha AL, Eger II EI, Tinker JR Determination and applications of MAC. *Anesthesiology* 1980; 53: 315-34A
44. Scheller MS, Saidman LJ, Partridge BL. MAC of sevoflurane in humans and the New Zealand white rabbit. *Can J Anaesth* 1988; 35: 153-6
45. Eger H EI. Partition coefficients of 1-653 in human blood, saline, and olive oil. *Anesth Analg* 1987; 66: 971-3
46. P. Vlisides P & Z. Xie (2012) Neurotoxicity of general anesthetics: an update., *Curr Pharm Design*, 18(38):6232-40, see [2], accessed 15 August 2015
47. Sun, L. (2010). "Early childhood general anesthesia exposure and neurocognitive development". *Br J Anaesth* 105 (Suppl 1): i61-8. doi:10.1093/bjaiae302
48. Pypendop H, Ilkiw JE. The effects of intravenous lidocaine administration on the minimum alveolar concentration of isoflurane in cats *Anesth Analg* 2005;100:97-101.
49. Bach FW, Jensen TS, Kastrup S, Stigsby B, Deigaard A. The effect of intravenous lidocaine on nociceptive processing in diabetic neuropathy.
50. Hans GA, Lauwick SM, Kaba A, Bonhomme V, Strays NEVI, Hans PC, et al. Intravenous lidocaine infusion reduces bispectral index-guided requirements of propofol only during surgical stimulation. *Brit J Anaesth* 2010;105:471-9.
51. Altermatt FR, Bugedo DA, Delfino AE, Solari S, Guerra Munoz FIR, et al. Evaluation of the effect of intravenous lidocaine on propofol requirements during total intravenous anaesthesia as measured by the bispectral index. *Brit J Anaesth* 2012;108:979-83
52. Gaughen CM, Durieux M. The effect of too much intravenous lidocaine on the bispectral index. *Anesth Analg*, 2006;103:1464--5.
53. Koppert W, Weigand M, Neumann F, Sittl R, Schuettler J, Schmelz M, et al. Perioperative intravenous lidocaine has preventive effects on postoperative pain and morphine consumption after major abdominal surgery. *Anesth Analg* 2004;98:1050-5.
54. Mostafa SM, Murthy IW, Hodgson CA, Besse E. Nebulized 10% lignocaine for awake fibreoptic intubation. *Anaesth Intens Care* 1998;26:222-3

